REMARKS/ARGUMENTS

I. Status of the Claims

This paper is filed in response to the Office Action mailed October 20, 2004. The amendments and remarks that are presented place the application in better condition for allowance or appeal. Applicant has amended claim 59, and added claims 74 and 75. Claims 1-58 and claim 63 have been canceled without prejudice or disclaimer. Applicant notes that the preliminary amendments filed with the application are somewhat confusing, as duplicates of previous preliminary amendments were also filed at the same time. Applicant directs the examiner's attention to the preliminary amendment dated September 24, 2001, wherein claims 29-58 were cancelled. If the Examiner does not have a copy of this amendment in the record for any reason, Applicant invites the examiner to contact the undersigned representative to resolve this matter. Support for the amendments can be found throughout the application, for example paragraphs 39, 41 and 56 of the specification.

II. Claim Rejections under 35 U.S.C. § 112

Claims 63-66 stand rejected under U.S.C. § 112 as reciting the limitation "starting material" in the first line of each said claim as there is an insufficient antecedent basis in claim 59

Applicant has amended claim 59 to recite a "starting material," rendering this rejection moot. Reconsideration and withdrawal is requested by the Applicants.

III. Claim Rejections under 35 U.S.C. § 102

Claims 59-64, 66 and 69-71 stand rejected under 35 U.S.C. §102(b) as being anticipated by Chan *et.al.*

The examiner states that Chan *et al.* disclose a homogenous, purified, unaltered alpha1-AT. The examiner further alleges that the protein was obtained by a process that is substantially the same as the claimed purification method.

Based on these statements, the examiner concludes that the purified alpha1-AT disclosed by Chan *et al.* is inherently the same as that disclosed by the instant specification.

The examiner argues that the claimed pI does not make the instant claims patentable over the prior art because the pI of the purified alpha1-AT is an inherent property of the molecule.

Applicant respectfully traverses the rejection, as applied to the claims as amended. As noted by the examiner, all claim elements must be disclosed expressly or inherently in the cited reference in order to anticipate a claim under 35 USC § 102(b). The Chan *et al* reference specifically notes that "Serum (300 ml) **from the same donor** was passed through a column . . ." Thus, the claim limitation of utilizing a starting material from pooled human plasma is not met in the cited reference. Applicants respectfully request reconsideration and withdrawal of this rejection.

With regard to new claims 74 and 75, the present invention is based on an advantageous purification method for alpha1-AT, comprising absorbing an alpha1-AT-containing fraction onto a chromatographic anion exchanger in the presence of a detergent. The use of a detergent as described in the present patent specification (e.g. section 45) is a crucial feature of the invention (see also Mattes, J.P. *et al*, (2001), Vox Sang 81: 29-36, in particular section "Results – alpha1-PI-purification", page 31).

In the method described by Chan *et al.*, no detergent is being used in the anionic chromatographic step nor is such use suggested in Chan *et al.*. The distinguishing feature "in the presence of a detergent " is added in the new claim 74 submitted herewith. The language of new claims 74 – 75 finds basis in sections 39 and 41 as well as in section 56 of the specification. In addition, as noted above, Chan *et al* does not utilize pooled human plasma as a starting material. The limitations of claims 74 and 75 are not met by the cited reference, thus the applicants respectfully request reconsideration and withdrawal of this rejection.

Furthermore, applicants respectfully traverse the assertion by the examiner that the alpha 1-AT isolated in the Chan *et al* reference is necessarily of a PI between 4.3 and 4.4. As noted in the data submitted by the applicants in Table 2 noting the isoelectric focusing gel bands, alpha 1-AT of PI's ranging from 4.35 to 4.58 are isolated using the methods of the invention. The examiner has presented no evidence or citation to substantiate the assertion that the PI 4.3 - 4.4 isomer was isolated by Chan *et al*, whose plasma fraction was subjected to repeated chromatography on DEAE cellulose under non-detergent conditions. Applicants invite the examiner to further substantiate the assertion, or to withdraw the assertion.

IV. Claims Rejections under 35 U.S.C. §103

Claim 68 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Chan *et al* in view of BioRad Catalog and Fitchmun (US 5,760,179)

According to the examiner, Chan *et al.* do not teach the employment of ceramic HAP for the disclosed alpha1-AT purification.

However, the examiner alleges that it would have been obvious for a person skilled in the art to replace the crystalline-Bio-Gel HAP used by Chan *et al* with a ceramic HAP with a reasonable expectation of success.

The Fitchmun-document is cited to show that Bio-Rad already supplied ceramic HAP at the time the instant invention was made.

Claims 65, 67, 72 and 73 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Chan *et al* in view of Lebing *et al.* (US 5,610,285)

According to the examiner, Chan *et al* do not teach using a Cohn fraction or blood as a starting material.

Furthermore, the examiner states, that Chan *et al.* do not disclose the employment of a detergent or heat to inactivate pathogens present in the preparation.

The examiner further states that Lebing *et al* teach the purification of alpha1-AT from a Cohn fraction and furthermore that it is important to inactivate viral pathogens that may be present in the plasma by adding a detergent to the chromatography or employing a dry heat or pasteurization step to the method.

With regard to amended claim 59 and dependent claims, applicant respectfully traverses the rejection. The Chan *et al* reference discloses a method for use in laboratory settings to purify a small amount of alpha 1-AT from a single individual. The disclosed purpose of this process is to isolate purified enzyme for chemical analysis (molecular weight, carbohydrate and amino acid composition) "from a single genetic type" (see discussion page 81 of the reference.) No mention or suggestion is made in the Chan *et al* reference of using the process for the production of alpha 1-AT for therapeutic use. In fact, the use of pooled plasma would frustrate the purported purpose of this reference in studying particular alleles of the protein.

Furthermore, the Chan *et al* reference does not indicate that the finished alpha 1-AT has an increased enzymatic activity as compared to plasma: thus inactive alpha 1-AT inherent in the plasma sample may still be present in the product of the Chan *et al* process. Given the Applicant's submission in Example 1 (see paragraph 69) wherein inactive alpha 1-AT is eluted at 100 mM phosphate, one would expect that inactive alpha 1-AT was eluted in the Chan *et al* process that utilized a wide gradient of 5 – 300 mM phosphate. Thus, the person of ordinary skill in the art would not have been motivated to utilize pooled plasma in the method of Chan *et al* to produce increased amounts of alpha 1-AT because the recited process is very cumbersome, and tailored to biochemical characterization of individual samples, and does not recite any substantial benefits to using this process over other purifications processes known in the art. Applicants respectfully request the reconsideration and withdrawal of the rejection.

With regard to new claims 74 and 75, Applicant respectfully traverses the rejection. The method specified in the presently filed new claims differs from the method described by Chan *et al.*, a key difference being the use of detergent in the anion-exchange chromatography. As noted above, there would have been no motivation for one of ordinary skill in the art to apply the method of Chan *et al* to a pooled plasma fraction. Thus, Applicant respectfully requests the reconsideration and withdrawal or this rejection on this basis.

In addition, although the examiner is correct in that Lebing teaches the purification of alpha1-AT derived from plasma, the only mention of detergent in Lebing *et al.* is as one of many alternatives for the inactivation of viruses. Moreover Lebing *et al* teach a method in which the viral inactivation step (in which detergent may or may not be used) is performed before a cation exchange chromatography (see drawing on page 1 as well as col. 3, lines 40-55 of the referenced patent). As described in col. 4, lines 4-11 and in Example I (col. 6, lines 11-12) as well as claimed in claim 1 of Lebing *et al*, the chromatography performed subsequent to the virus inactivation step is carried out under conditions in which alpha1-AT does not bind to the column. In contrast, in the instant invention, the detergent is added not only for a different reason but also before adding the fraction to an anion-exchange column, and the alpha1-AT binds to the column (see e.g. section 40). Therefore, the feature "comprising

absorbing an alpha1-AT-containing fraction ... in the presence of a detergent" of new claim 74 is not mentioned nor suggested by Lebing *et al*. Thus, applicants respectfully submit that even in combination, the cited Chan *et al* and Lebing *et al* do not suggest the limitations of the claims. Applicants further respectfully request the reconsideration and withdrawal of the rejection on this further basis.

CONCLUSION

In view of the foregoing, applicants believe all claims now pending in this application are in condition for allowance and an action to that end is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 323-644-9845.

Respectfully submitted,

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